PLASMA FOR GREAT BRITAIN*

? 1940

On the day that the first massive bombings of London took place August 16, 1941, the Blood Transfusion Association of New York, formerly known as the Blood Transfusion Betterment Association, with the cooperation of the American Red Cross, launched a project unlike any other ever attempted in the annals of medical history. This project consisted of collecting blood from the civilian population of greater New York, removing the plasma, and shipping it across the Atlantic for use by the British in the treatment of both civilian and military war casualties.

A preliminary report of the difficulties as well as the favorable aspects of this work was published by the Blood Transfusion Association on January 31, 1941. It is unnecessary to recount here the things already reported there in considerable detail, but it is perhaps worthwhile to recapitulate in brief the history of this movement in order that some of the final results to be reported today may have more meaning.

During the winter of 1939-1940 an appropriation was made by the Blood Transfusion Association to Dr. John Scudder of the Presbyterian Hospital for the purpose of carrying out studies of a laboratory and clinical type related to the preservation of and the use of plasma as a blood substitute. Associated in this work were Dr. Charles R. Drew and Dr. Kingsley Bishop.

While this work was being carried on Dr. Allen O. Whipple, Chief of the Surgical Service at the Presbyterian Hospital in New York, was called upon to fly to Italy to act as a surgical consultant for an emissary of the President in Rome. (MYRON C. TAYLOR) He requested that plasma be prepared which he could take with him for use should the need arise. This was done.

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During the early days of the attack on France Dr. Alexis Carrel told to a group called together by Mr. John F. Bush, President of the Blood Transfusion Association the need of some means of treating these patients and suggested the use of plasma or serum as the most logical way. Dr. Scudder suggested to Mr. Bush that the shipping of plasma to France was a plausible procedure and that it would be in line with the policies of the Blood Transfusion Association to extend their scope to such a worthwhile project. This the Medical Board of the Association agreed with and plans were made to enlist the aid of the voluntary hospitals in New York City in collecting and preparing plasma for trans-shipment. France, however, fell before the German army so rapidly that there was insufficient time to get this aid to them.

The idea had been born, however, and the American Red Cross had agreed to aid in financing such a project should any of the Allies need such assistance.

When word was received of the great losses of the British, in their withdrawal from Dunkerque, and informal news was received to the effect that the B. E. F. had sustained heavy losses in their mobile transfusion units, the Blood Transfusion Association attempted to ascertain whether plasma from this country would be of any assistance to them. The answer came back in the affirmative.

In July and early August, directed to a large extent by Mr. Tracy S. Voorhees, President of the Long Island College Hospital, and legal adviser to the Blood Transfusion Association, plans were inaugurated for the reception of donors and collection of blood in six voluntary hospitals. These were as follows: Presbyterian, New York, Memorial, Mt. Sinai, Post Graduate, and Long Island College. Later three others joined in this work. They were:

Lenox Hill, the Hospital for Joint Diseases, and the Jewish Hospital of Brooklyn.

It is impossible to give adequate credit here to the great number of individuals, both medical and non-medical, who gave their unstinted efforts, in many cases at great personal sacrifice to this new type of humanitarian medical experiment. Over two thousand doctors, nurses, technicians, social workers, Red Cross volunteers,and enthusiastic laymen cooperated to make this dream an actuality. A few, however, should be mentioned. Among them are: Mr. John F. Bush, President of the Blood Transfusion Association, whose enthusiasm and wise guidance made such a scheme possible. He was more than ably assisted in all the phases of the work by Mr. Tracy S. Voorhees. Dr. DeWitt Stetten, Vice-President of the Association and Chairman of the Board of Medical Control, was equally effective. The Plasma Committee had as its chairman Dr. C. P. Rhoads, Medical Director of the Memorial Hospital. Ably assisting him as members of this committee were: Dr. David C. Bull of the Presbyterian Hospital and Dr. Lester J. Unger of the Post Graduate Hospital and Dr. John Scudder.

When it became apparent that a central depot would be necessary in order to coordinate the in-coming calls, distribute the donors to the various hospitals, keep a record of the entire procedure, and coordinate shipping with the American Red Cross, space and facilities were donated by the New York Academy of Medicine in its building. Mr. Morris M. Davidson volunteered to serve as a full-time director of the many administrative details of this project and Dr. Charles R. Drew was appointed as full-time Medical Supervisor. It became the latter's duty to coordinate the medical aspects of the program, to establish uniform records, standard equipment, and suitable technical criteria to insure the safety of the final product.

Infection, either early or late, became the one dominant problem. To assist in controlling this phase of the work Dr. Frank L. Meleney, assisted

by Miss Balbina Johnson, offered the services of his laboratory as a central testing depot of all material before final shipment.

Worthy of especial notice also are: Dr. Nathan Rosenthal, Director of the Department of Hematology at Mt. Sinai Hospital, who organized a unit which did over 3,000 phlebotomies and established an unusual record for the total percentage of the blood collected which passed all tests and was shipped to England in the form of plasma-saline; Dr. Lester J. Unger, in addition to directing the Blood Banks at the Post Graduate Hospital and the Hospital for Joint Diseases, carried out important experiments throughout the project for the purpose of improving the technique; Dr. Ralph G. Stillman directed the project at the New York Hospital, Dr. E. R. Marzullo at the Long Island College Hospital, Dr. Perry J. Manheims at the Lenox Hill Hospital, and Dr. Alexander S. Weiner at the Jewish Hospital.

Dr. William Thalhimer offered not only his services but in association with Dr. Ralph S. Muckenfuss, Director of the Bureau of Laboratories of the Department of Health of the City of New York, offered the facilities of the Manhattan Convalescent Serum Laboratory for a large part of the experimental program.

Dr. E. H. L. Corwin, Managing Director of the Blood Transfusion Association, not only served on the committee with Dr. Scudder and Dr. Drew which outlined the organization but also carried much of the administrative load until Mr. Davidson took over this task as a full-time responsibility.

There are many others, unnamed who probably are as worthy as the above of special commendation but the limits of this paper do not allow a recitation of their contributions to this work.

FINAL RECORD OF PLASMA-SALINE PREPARED AND SHIPPED

All plasma shipped to England was diluted with an equal volume of physiological saline. This was done for several reasons, among them: (1) precipitation of the proteins especially fibrinogen takes place more slowly in the presence of saline. It was hoped that this would make it unnecessary to filter the solution before use. This, however, was not the case. (2) It was felt that by filling the flasks to the top denaturation of the proteins would take place more slowly. (3) It was felt that since the use of sodium chloride in solution has a beneficial effect upon the constricted arteriolar vessels in shock that it might enhance the value of this fluid for such treatment. (4) The concensus of opinion expressed at the meeting of the American Human Serum Association held in New York June 10, 1940 was that the safest blood substitute at that time was considered to be diluted plasma. All results therefore in the following Table are described in terms of plasma-saline solution. Each 1,000 c.c. Baxter Plasmavac contained 500 c.c. of plasma and 500 c.c. of physiological saline and sufficient "Merthiolate" (Lilly) to give a final concentration of 1:10,000. The shipments from the various hospitals were as follows:

TABLE I

TOTAL PLASMA-SALINE PREPARED AND SHIPPED

Hospitals	Plasma-Saline Prepared (in liters)	Plasma-Saline Shipped (in liters)
Presbyterian	1,547	1,464
Mt. Sinai	1,298	1,258
Post Graduate	930	888
New York	658	610
Long Island College	549	405
Joint Diseases	308	308
Memorial	216	198
Lenox Hill	190	190
Jewish	51	51
TOTAL	5,747	5,272

The difference between the amount of plasma prepared and passed by the individual hospitals as suitable for shipment and the amounts actually shipped represents the quantity found unsuitable by the Central Laboratory. This quantity equals 475 liters or 8.2% of the total quantity.

FINAL REPORT ON PLASMA-SALINE LOST

The greatest loss was due to contamination. There was no hospital in which some contamination of the final product was not discovered. These findings were entirely contrary to expectations and to those of investigators who had previously reported on preparation and use of plasma. It served to demonstrate that the mass production of human biologicals is not a simple procedure, free from danger. It soon became evident that a one-week incubation period was not sufficient to guarantee a sterile product several months later. The experience was had on repeated occasions that samples of plasma which had been passed after a two-weeks observation period were found at the end of a month to contain growing organisms. Many authorities were called in to discuss this very discouraging observation and out of it came the first steps on the part of the U. S. Public Health Service to change the regulations regarding the preparation and testing of human plasma which have now been put into effect.

A summary of the losses follows. Letters were used to represent the cooperating hospitals rather than the names. There is no desire to indict any particular institution but rather point out the difficulty had by all and thereby make more strong the point that in the preparation of human plasma great care must be exercised at each step of the procedure.

TABLE II.

PLASMA-SALINE LOST THROUGH CONTAMINATION AND BREAKAGE

Hospitals	Discarded at Hospital (in liters)	Discarded at Central Lab. (in liters)	Total Discarded in Percentage	Loss Through Breakage, Clotting, etc. (in liters)	Percentage, Breakage, etc.
A	251.6	183.0	24.3	17.8	1.1
B	9	40	3.7	31.5	2.4
C	56	42	9.9	7.1	0.76
D	12.4	48	9.0	3.2	0.48
E	8	144	27.3	3.2	0.58
F	8	0	2.5	0	0.0
G	16	18	14.7	0	0.0
H	20	0	9.5	1.4	0.73
I	0	0	0	2.5	4.9
TOTALS	385.0	475	14.0*	69.4	1.1

*The total loss reported includes not only infected plasma but also plasma discarded because of suspected contamination or known break in technique even when cultures were returned with negative reports.

LOSS DURING SHIPMENT

Only one boat was sunk during the life of the project which had aboard plasma-saline solution. This was the Western Prince which went down off the coast of Ireland in December carrying with it, among other things, 222 liters of plasma-saline solution.

DISTRIBUTION OF PLASMA IN GREAT BRITAIN

For many months it was very difficult to get reliable information from England as to what happened or was happening to the plasma which had been sent. So much was this so that there were doubts in the minds of some individuals as to whether the blood which they gave for England actually ever got there. I should like to insert at this point parts of a letter from Mr. P. L. Oliver, Honorary Secretary of the British Red Cross Transfusion Service, which is in the nature of a report to him from Dr. E. Bruce White of the National Institute for Medical Research at Hampstead, and shows with what great care the plasma was handled when it got to England.

"INSPECTION AND CONTROL TESTING OF THE AMERICAN RED CROSS SALINE PLASMA AT THE NATIONAL INSTITUTE FOR MEDICAL RESEARCH, HAMPSTEAD: RESULTS TO DATE. (APRIL 13, 1941)

"A. General Procedure.

"Notification to expect the arrival of a consignment of Plasma is received from the British Red Cross. On arrival the cases are checked, their seals examined, and any evidence of gross damage noted. The cases are stored - from lack of more suitable accommodation - in a cool basement corridor where they are under constant supervision.

"At unpacking: the case, carton and bottle identification marks are recorded, the gummed and usually cross-stamped hospital seals of the cartons being examined.

"In the case of rare breakages the affected cartons are cleaned so far as possible and dry-steam autoclaved. The solid bottles of plasma are sponged with Dettol and allowed to dry off in the air before replacement. Solid literature and accessories included in the cartons are precisely replaced by materials withdrawn from other cartons and referring to bottles which have been withdrawn for bacteriological testing. Every effort has been made to restore the affected cartons to the "chaste" condition in which they were issued. The empty slots are packed with paper, a record of the breakages is pasted within and without the carton.

"The bottles are individually examined in a good light - and any abnormalities recorded. Any specimens deemed necessary for bacteriological tests having been taken, signed notices of the removal of such bottles are pasted outside and inside the cartons and the vacant slots are packed with paper.

"When bacteriological testing is complete the cartons are resealed with gummed paper tape in the original manner and cross stamped "National Institute for Medical Research, Hampstead, N. W. 3" and "Medical Research Council, Emergency Public Health Laboratory Service."

"The Hospital label is, of course, left intact.

"The cartons are then replaced in their appropriate case and dispatched according to instructions received. No transfer of bottles from carton to carton or of cartons from case to case has been made."

"According to the Hospital of origin the cartons have been disposed of as follows: -

	No. of Cartons
Presbyterian Hospital	68

	No. of Cartons
Mount Sinai Hospital	89
New York Hospital	27
New York Post Graduate Medical School and Hospital	37
Long Island College Hospital	22
Memorial Hospital	18
Hospital for Joint Diseases	6
Lennox Hill Hospital	7

"Certain Errors and Defects

"The following notes are made in no captious spirit but simply for information.

"The earlier labelling in which the Presbyterian Hospital gave a serial bottle number without the pool number while the Mount Sinai and other hospitals gave a pool number without hospital serial bottle number has we note with satisfaction been replaced by a system in which both pool and bottle numbers are stated.

"It has been noted that in a number of instances where 500 c.c. of plasma and 500 c.c. of sodium chloride solution are declared on the label (total 1000 c.c.) the contents do not exceed 750 c.c.

"Appearance of the Plasma Saline

"The bottle contents have varied considerably in appearance. Some have been almost liquid and deposit-free and, of the main contributors, the Mount Sinai Hospital seems to have been most fortunate in this respect. Many bottles, particularly those first received have shown a soft fluffy deposit forming a layer 1/4 in. (or more) deep at the bottom; such appearances have been rare in

the consignments more recently received. A few of the bottles have shown extensive clotting (see Tables I and II) and have in all cases been found heavily contaminated with bacteria.

"Procedure in Bacteriological and Toxicity Testing.

"The tests have been performed so far as possible with precautions adequate to the problem.

"No attempt has been made to neutralize the merthiolate present as this would have involved a preliminary research for which time is not available. In place, a small inoculation (0.2 c.c.) has been made into a large volume of nutrituve medium (200 c.c.) to reduce the merthiolate concentration to 1:10,000,000. We think the method though costly in media has been very adequate.

"The test media have been Hartley's broth for aerobic tests and for anaerobic culture the same medium, vaseline covered, with coagulated meat and 0.2% of added glucose.

"The bottles are incubated for 5 days at 37° and are then, if negative, observed for a period at room temperature.

"Direct platings are made on agar (or blood agar) and stained films of the plasma are examined microscopically.

"In a number of cases 1 c.c. or 2 c.c. amounts have been subcutaneously injected into mice; it may be said forthwith that no toxic symptoms have been noted.

"Results of bacteriological tests.

"A list of the bottles examined is given below and the results of the tests summarized in Tables III and IV. The items are classified in what we believe to be the manner giving the fairest presentation of the facts.

"During the latter period of the testing in view of the satisfactory nature of the results of the number of bottles taken for examination has been reduced to a minimum and we have been guided in the choice of samples by those appearances which suggested possible contamination. It has been felt improper either to waste valuable material for the sake of formality or to issue under the hospital label any bottle with which we have interfered.

"It will be seen from the tables that the first period was one of some anxiety in that, of the 17 samples received from Dr. Heyl, Dr. Harrison and taken from the cases 7605/1M - 7605/4M, no fewer than 7 and possibly 8 gave growth in culture media. The 8th case was doubtful in that a second sample gave negative results while in the case of 6 others tested a second time confirmatory results were obtained. In the case of Dr. Heyl's bottle a rice growth - confluent in direct culture on agar? - of Staph. aureus was obtained.

"The contents of cases 7605/1M - 7605/4M have been withheld from circulation.

"The second period has been one of almost unbroken satisfactory results: the only untoward finding being in the case of the bottles forming pools 29 and 33 which were all heavily contaminated with gram negative bacilli of coliform type and showed varying degrees of clotting.

"The cases which we have marked 001 - 006 and the great majority of the 62 cases marked with numbers between 1 and 96 have now been forwarded to the transfusion centres. It is hoped to inspect and clear the remaining cases in hand during the next fortnight.

(Signed) P. Bruce White"

TABLE III.

Results of Some Preliminary Examinations Not Readily Incorporated in Main Table IV.

Carton No.	Bottle No.	Bacteriological Test	Remarks
?	155	Positive (Bact. proteus Streptococci Gm - bacilli)	Very heavy contamination - extensive clotting
12	146	Negative	
14	140	Negative	
17	157	Positive (Staph. aureus)	Very heavy contamination - turbid - much sediment.
9	62	Positive (diphtheriods)	A hospital label was lacking - #62 in pencil on small label - low grade contamination

Examined - 5 bottles

Found contaminated - 3 bottles (2 being gravely infected)

TABLE IV*

Results of Main Series of Bacteriological Tests

(* - 1 leaking through broken needle inserted in stopper. 1 with airlead tube broken. 1 unlabelled.)

Hospital	No. of Cartons	No. of Bottles	No. of Bottles Broken	Bottles Found Defective	No. Tested Bacterio-logically	Bottles Found Contaminated	
						No.	Details
4 CASES MARKED 7605/1M - 7605/4M							
Presbyterian	10	60	-	-	9	2 (3)	C32 - 184 (anaerobic gram - cocci) C33 - 191 (anaerobic strepto-cocci) C34 - 198 (large gram - cocci) not confirmed at 2nd trial.
Mount Sinai	6	36	-	-	3	2	C1 - P8 - N. T. E. 02739 (diphtheroids) C3 - P10 - N. T. E. 02578 (anaerobic gas forming cocci and diphtheroids)
	16	96	-	-	12	4 (5)	
6 CASES NUMBERED HERE 001 - 006 - 62 CASES NUMBERED BETWEEN 1 and 96 (see above)							
Presbyterian	58	348	2	-	17	-	
Mount Sinai	83	498	1	3*	13	-	
New York	27	162	-	-	4	-	
New York Post Graduate Med. Sch.	37	222	1	-	3	-	
Long Island Col.	22	132	1	-	10	6	6 bottles of Pools 29 and 33 in Cartons 19 and 20 heavily contaminated gram-coliform bacilli - much clotting
Memorial	18	108	-	-	2	-	
Hospital for Joint Diseases	6	36	-	-	1	-	
Lennox Hill	7	42	-	-	2	-	

*(These cartons were those shipped before the establishment of a central control laboratory)

The Blood Transfusion Association started this project with but two purposes:

1. To lend immediate aid for war casualties in Great Britain;
2. To gather information which would be of value to the armed forces of the United States in case of a national emergency.

This report from the British Red Cross does show that the first purpose was, to some extent, fulfilled. It perhaps needs a little explanation. The first period referred to in Dr. White's report refers to the period of time during which each hospital was responsible for the complete running of its part of the program. Standards were different. Equipment was markedly different. Culture methods were different and personnel in some cases was very poorly equipped to carry out such a technical procedure. The second period refers to the time dating from the establishment of a central administrative office, a full time medical supervisor, and a central bacteriology laboratory to act as a check on the individual hospitals. Likewise during this second phase of the work full time technicians were provided for in each hospital and the period for observing cultures was lengthened from two weeks to three weeks before any particular sample was released for shipment. In this second phase one batch of infected material did, by mistake, get shipped to England. The authorities there were notified of this suspected shipment and, as shown in the report, it was picked up on the other side. We feel that with the triple check on this material no harm has come to any of the recipients and there is increasing evidence, in the form of letters or direct contact with men returning from overseas, that the material sent has been put to good use. Out of this experience the following routines were determined to be adequate for bacterial culture and were supplied to each hospital.

DIRECTIONS FOR CULTURING PLASMA

I. ROUTINE TO BE FOLLOWED IN THE LABORATORIES OF THE COOPERATING HOSPITALS.

When plasma has been removed from 8-12 recipient bottles (depending upon the size of the pooling flask), 10 c.c. of each pool is withdrawn into a sterile pipette for culture.

A. Aerobic Cultures:

5 c.c. of the plasma from each pool is inoculated into an 8x1 inch tube containing 35 c.c. of a modified Holman's 0.2% dextrose cooked meat medium. This medium is prepared as follows:

Stir 1 lb. of very fresh lean chopped beef heart into 1 liter of water (distilled preferred). This infusion should be left in refrigerator overnight.

Boil vigorously for 15 minutes. Strain through cheese cloth and restore to original volume with distilled water.

Add: Neopeptone (Difco) 1% (10 grams)
NaCl 0.5% (5 grams)
and stir until dissolved.

For Dextrose Meat Medium

Adjust pH to 8.4.

Boil for 20 minutes, restore to original volume with distilled water, filter through paper until clear.

Add 0.2% dextrose.

The chopped cooked meat is washed in strainer under running water to remove fine particles, allowed to drain, and excess water squeezed out.

The cooked meat medium is to be distributed into tubes, 8" x 1", filled ½ full with cooked meat, and at least 35 c.c. of broth added.

Tubes are autoclaved at 15 lbs. pressure for 30 minutes. Final pH should be 7.4 to 7.6.

B. Anaerobic Cultures:

5 c.c. of the plasma from the pool is incubated into an 8" x 1" tube containing 40 ccs. Brewer's dextrose Thioglycolate medium (J.A.M.A. 115:598, August 24, 1940). This medium may be procured from the Baltimore Biological Laboratories in Baltimore, Md. It contains:

Pork Infusion solids (from 37.5 gms. pork)	1.0%
Peptone-Thio	1.0%
Dextrose	1.0%
NaCl	0.5%
Sodium Thioglycolate	0.1%
Agar	0.05%
Methylene Blue (1:500,000)	0.0002%

Dissolve 3.65 grams in 100 cc. of distilled water. Heat until the solution boils and allow to boil about one minute. Autoclave 20 minutes at 120° C., 40 cc. to each tube. Do not store the powder in the refrigerator because this decreases the duration of anaerobiosis.

Both tubes are to be inoculated at 37° C. for two weeks. Examination of standard preparations of these tubes are to be made after 3, 7 and 14 days. If bacteria are seen on stained preparation, transfusions of 0.5 cc. are to be made to fresh 0.2% dextrose cooked meat media. (Tubes 6" x 5/8"), and 0.2 cc. is to be transferred to each of two blood agar plates, one for aerobic incubation and the other for anaerobic incubation. The organism should then be identified.

If at the end of 72 hours all cultures from each pool are negative, then that pool may be dispensed into final containers. If the 7-day or 14-day examination shows evidence of contamination not found at 72 hours, this should be reported to Dr. Meleney's Laboratory at the Presbyterian Hospital. Otherwise it will be assumed that the pool was free from contamination.

If the 72-hour examination of the pool shows a contaminant in both tubes, the pool is immediately discarded. If there is a contaminant in only one of the two tubes, 22 ccs. of this pool should be recultured (10 cc. aerobically and 10 cc. anaerobically). If after one week these cultures are sterile, the pool may be bottled.

II. DISTRIBUTION OF POOL INTO FINAL BAXTER PLASMAVAC BOTTLES.

Immediately following the withdrawal of the sample of plasma from the fresh pool for culturing, there should be added to each pool sufficient fubbered 1-100 Merthiolate to form a dilution of 1:10,000 Merthiolate in the final plasma saline mixture. The safest way to be sure of the right proportion is to add 40 ccs. of a freshly prepared 1% solution to each pooling flask containing 2,000 ccs. of plasma. A simpler method is to add 10 ccs. of a 4% solution of Merthiolate to each 2,000 ccs. pooling flask.

It has been suggested that the Merthiolate powder be added to sterile distilled water and buffered by means of chemically pure sodium borate in the ratio of 1 gm. Merthiolate to 1.4 gm. sodium borate per 100 cc. distilled water. Or, in case of the stronger solution, 4 gm. Merthiolate to 5.6 gm. of sodium borate per 100 cc. distilled water.

Such pools are then set aside in the refrigerator until the 1 week culture reports are returned. If these reports are negative, then each pool may be dispensed into the final containers. Each Plasmavac contains 500 cc. physiological saline, to which is added 500 cc. of the pooled plasma. The last 35 cc. of plasma in the pool is run into a special control bottle containing 35 cc. of normal saline from the same batch of normal saline used in the Plasmavacs. This special bottle is to be labelled with the date, the name of the hospital, the number of the pool, and the

carton number in which the pool is packed. These control bottles will be sent with the carton to the warehouse where a messenger will pick them up each day to carry them to the central laboratory, which is situated in the surgical bacteriological laboratory of the Presbyterian Hospital. Here rechecks of the pools will be done at one-week, and two-week intervals, before the cartons are finally released for shipment, a total period of observation of one month.

III. POSITIVE CULTURES IN CENTRAL LABORATORIES FOLLOWING NEGATIVE CULTURES IN HOSPITAL LABORATORIES.

Should a positive culture be obtained in the central laboratory on a plasma pool which has already been released by the hospital and sent to the store-room, the whole pool will be brought to the central laboratory and each flask in that pool will be separately cultured. The hospitals therefore should have readily available records of the serial numbers of of the plasmavac bottles which were put up from any given pool.

The same procedure will be carried out if the two-week findings on the individual hospitals should be positive following a negative one week culture. This information is to be transferred to the central laboratory at once so that such pools may be retrieved from the storehouse and recultured.

IV. TOXICITY TEST.

In order to add a factor of safety and to come within the spirit of the law, one mouse will be injected intra-peritoneally with 1 cc. of plasma from each control bottle, and observed for 72 hours. It is not necessary for this toxicity test to be done by the individual hospitals.

COST OF PROJECT

The total cost of this project covering cash receipts and cash disbursements for the period from June 26, 1940 to March 28, 1941 was $42,087.24. Of this total $132.00 was received from individuals who took this means of assisting in Britain's fight. Of the remaining $41,955.24 the American Red Cross contributed two-thirds or $27,970.16, the Blood Transfusion Association one-third, $13,985.08.

While the full responsibility for the collection and preparing of the plasma was the function of the Blood Transfusion Association all arrangements for shipping and for dispersal in England were taken care of by the American Red Cross. Mr. Norman Davis took a very personal interest in this unusual effort as did Mr. DeWitt Smith and Dr. William DeKline of the National Office in Washington. To Capt. Charles B. Scully of the Red Cross Lifesaving Service, assisted by Colonel L. Boothe, fell the tremendous job of supplying the hospitals with an endless stream of donors, at times as many as 300 a day, for a period of approximately five months. At the end of this time word was received from England that their equipment and organization was sufficient to their needs and that this project in America might be brought to a close.

COST PER LITER OF PLASMA-SALINE DELIVERED TO ENGLAND

In determining the actual cost of production it must be remembered that the individual hospitals spent large sums of their own funds in order to set up a collection center which would meet the requirements of the Board of Medical Control of the Blood Transfusion Association before that hospital was considered as a cooperating unit in the project. These costs, of course, do not show and are not known exactly but the average outlay per hospital was in the neighborhood of $3,000.00 for equipment.

In order to lessen the burden to some extent each hospital was paid the sum of $1.50 for each liter of plasma-saline released for shipment. This amounted to a total of $7,908.00 and is included as one of the items in the total disbursement of $41,353.08. Using this total figure and the figure 5,272 liters as the total amount shipped the cost per liter of plasma-saline was $7.84. This represents a cost of $15.68 per liter of undiluted plasma. This compares very favorably with the current commercial price of plasma which in different localities and institutions varies between $60.00 and $100.00 per liter. The difference is due to the fact that the blood was given and most of the labor of a volunteer character.

RELATIONSHIP OF PROJECT TO THE NATIONAL RESEARCH COUNCIL AND THE COUNCIL FOR NATIONAL DEFENSE

From the very beginning of the project, its second purpose as stated above was to secure all the information possible concerning the preparation and use of blood substitutes which might be of use to this country in case of a national emergency. To this end Dr. Walter B. Cannon, Chairman of the Blood Transfusion Committee of the National Research Council, and Dr. Cyrus C. Sturgis of Ann Arbor, Chairman of the Sub-Committee on Blood Substitutes, were advised of each step in the procedure and their advice was sought especially in reference to the research problems which presented themselves. It is perhaps in the experimental work which has grown out of this project that the greatest good will have been done.

EXPERIMENTAL PROBLEMS

Neither the literature nor past experience provided the answers to some of the problems which arose during the project. Among these problems were:

the best type of container for the collection of the blood; the safest apparatus for transferring the plasma from the donor bottles to the pooling flasks; the possibility of filtering plasma through a bacteria filter; the best bacteriostatic agent for preserving the plasma; the proper and safest period of observation of the cultures in order to insure complete long time sterility; the toxicity of plasma when compared to serum; the efficacy of plasma as a blood substitute when compared to serum; the toxicity and efficacy of dried plasma or serum when compared with liquid plasma or serum; the most suitable apparatus for drying plasma or serum; and the nature of the changes brought about by the various methods of drying plasma or serum.

At this time no final answer can be given to all of the questions that arose but certain conclusions are available as the result of work which has been carried on by several investigators related to each of the above noted problems. Taken in order they may be stated briefly as follows:

1. Donor Bottle. It is the concensus of opinion of most of the men who worked in this project that the ideal donor bottle should be as narrow as is compatible with stability, that it should hold between 550 and 600 cc., that it should be capable of being centrifuged, that it should be made of high quality glass, that it should be fitted with a stopper and attachments which would allow the collection of blood and the removal of plasma without exposure of the fluids to air, i.e., in a completely closed system. No such bottle was available during the progress of this project. Several attempts were made to create such a bottle and either the primary cost of the mold, the inability to get centrifuge heads to fit or adequate capping devices prevented the realization of this part of the program. Since the closing of the program several of the larger commercial intravenous fluid dispensing

companies have interested themselves in the creation of such a bottle. The virtues of such a bottle are: the slower rate at which the cells degenerate, the increased yield of plasma, the increased freedom from infection, and the increased saving in refrigerator space.

2. Pooling of Plasma. It was found that when the plasma from eight individuals of different blood groups were pooled in just about the same proportion as the different blood groups occur in the population as a whole that the resulting titre was never sufficiently high to cause coagulation of the recipient's cells. This criterion we feel to be a safe one. Complete suppression of agglutinins may be brought about by using larger pools.

The Board of Medical Control at first earnestly requested and later demanded that hospitals taking part in the program provide a dust-proof hood or room, preferably air conditioned and bathed in ultraviolet light, for the pooling of plasma. It was further recommended that persons removing the plasma from the blood and pooling it and then distributing the pooled plasma into the final containers use surgical technique throughout including the wearing of sterile gloves, gown, cap and mask. It was also recommended that where suction for pooling is created by a motor and pump that there be a water trap interposed in the line in order to prevent a backwash of contaminated air. And that the plasma have interposed in the line between the donor bottle and the pooling bottle a stainless steel 120-mesh filter.

3. Filtration of Plasma. Contaminated plasma picked up early in the project suggested that an added safety factor would be the filtering of all plasma before final dispensation. This proved a difficult job. The fibrinogen content of the plasma made filtration through the ordinary diatomaceous earth or porcelain filter in large quantities an impossibility. When an attempt was made to filter it through a Seitz filter it was found that for

a while the filtrate was clear but that later on, beginning with the last portions filtered, not only was there the typical fibrin precipitate but actual clotting in the absence of infection. Several investigators began to work on this problem. Some interesting data was compiled. It appears that the fine asbestos fibers in the Seitz filters are enmeshed in a wood pulp reticulum which is very rich in calcium in loose formation. This was a source of difficulty, first, by causing a rapid precipitation of fibrinogen on the pads thereby clogging the pores and soon bringing the whole procedure to a stop. Secondly, much of the calcium was dissolved or washed through by the plasma so that the calcium content of the filtered material often was increased 200 to 300 percent above the level of the unfiltered material. This, it is thought, played some part in the formation of the jelly-like clot which was so often seen in the filtered material. Finally, it was felt that a part of the sodium citrate was removed from the plasma by the filter pads. To irradicate this source of trouble three things were done: (1) filter pads were created by the Seitz Company which were practically calcium free, (2) when these pads were set up in the filter racks a solution of 1/10 N hydrochloric acid was passed through the filters to fix any small quantities of calcium which might have been present. These pads were then washed with distilled water to remove the excess acidity. (3) As a final step a solution of weak sodium citrate was run through the pads with the hope that the suspected absorption of citrate from the plasma might be prevented by this pre-treatment with citrate . This piece of research is to be made the subject of a special presentation by Dr. Lester J. Unger when his studies are complete.

4. Separation of Plasma by Cream Separator Type of Centrifuge. When it became apparent that the syphoning off of plasma, bottle by bottle, would always

be a rather slow and tedious procedure, ways were sought in which the separation might be done more rapidly. Having heard that a centrifuge of the Cream Separator type had been successfully used in England inquiries were made at the several centrifuge manufacturing concerns with the idea of having one of the cream separators modified so that it might separate cells from plasma in one continuous stream thereby greatly speeding up the production of plasma. Such a centrifuge was obtained from the DeLaval Company and set up in the laboratories of the Manhattan Convalescent Serum Association and there tried out. It has had insufficient trial on large scale production to unqualifiedly recommend it for continuous mass production of plasma at this time but small batches of blood have been run through it and the resultant plasma has been free from both hemolysis and cells. This modified cream separator was connected to a specially constructed collecting chamber in which the plasma was pooled and from which it was forced with carbon dioxide under pressure through the large Seitz filters. Properly adjusted this series of pieces of apparatus might well solve the problem of mass production of filtered plasma should the need arise.

5. Bacteriostatic Agent for Preserving Plasma. In the beginning of the project since bacterial filtration was not contemplated it was decided to use some bacteriostatic agent. The agent of choice was "Merthiolate" (Sodium Ethyl Mercuri Thisalicylate, Lilly). Its use was not entirely satisfactory and Mr. W. A. Jamieson, Director of the Biological Division of the Lilly Research Laboratories, was good enough to confer with us in New York on several occasions about this matter. Dr. Meleney and Miss Johnson have reported at some length in an earlier part of this program on this phase of the work. I should like to correct here a statement attributed to Mr. Jamieson which occurred on page 51 of the Report of the Blood Transfusion Association. The

statement was: "I agree with Dr. Meleney that in order to have cultures of any value, once the Merthiolate has been added, the plasma saline mixture would have to be neutralized and Dr. Meleney's suggestion that 1 cc. of 1% ammonium sulfide be added to each 10 cc. of plasma and 50 cc. of the media, I believe is a good one. The ammonium sulfide will precipitate mercury and render it inert." Mr. Jamieson tells me that this is an incorrect statement. He has set up experiments to test this statement and finds that the ammonium sulfide will not precipitate the mercury in "Merthiolate" and will not render it inert in the dilution which is present in "Merthiolate." I bring this before you at this time in order that your time may not be wasted in attempting to neutralize "Merthiolate" with ammonium sulfide before culturing plasma so preserved. For a more complete discussion of the bacteriostatic action of "Merthiolate" I refer you to the earlier paper of Dr. Meleney and Miss Johnson.

When we received communication from Dr. Milan Novak of the University of Illinois of his successful maintenance of the sterility of blood plasma by the use of sulfanilamide we requested Dr. Alphonzo Dochez of the Presbyterian Hospital to allow two of his residents and assistants, Dr. William Province and Dr. Fred Heath, to repeat Dr. Novak's work with the idea of making use of this method in the project. This problem proved more difficult than it first appeared. And at this time these investigators are not ready to give a final report. Such, however, will be published in the very near future. We do, however, recommend the works of Dr. Novak for your consideration.

6. Element of Time in Study of Bacterial Cultures. Dr. P. Bruce White, in his letter quoted above, stated: "It will be seen from the tables that the first period was one of some anxiety in that, of the 17 samples received from Dr. Heyl, ... no fewer than 7 and possibly 8 gave growth in culture media." If this was a period of anxiety for Dr. White it was a period of greatest

distress for the Blood Transfusion Association and a matter of real concern for the U. S. Department of Health, especially the Division of Biologics. The rules concerning the culturing and testing of biologics had been carefully followed and negative cultures had been reported before shipment on each of these bottles which was later found contaminated. This cabled report from England seemed to threaten the whole project and was the cause of a great raising of standards of preparation on the part of all concerned.

When the Central Laboratory was established and pilot tubes from each final container were followed for at least three weeks before a negative report was turned in and the plasma released for shipment, only one infected sample reached England and the authorities there were advised of this possibility before the material arrived. The essence of this paragraph is that the present methods and criteria of establishing positive or negative cultures, as routinely carried out in most hospital laboratories, are entirely inadequate in such a large scale project as the one under discussion.

7. Plasma vs. Serum. When it became obvious that there was a difference of opinion in the minds of qualified observers as to the relative merits of plasma and serum as blood substitutes a rather large scale experimental program was set up in New York in an attempt to gather real data on this most important problem. Arrangements were made whereby Capt. Charles B. Scully and Col. Earle Boothe of the American Red Cross were to supply donors to Dr. C. P. Rhoads at the Memorial Hospital with the clear instruction to the donors that they were giving their blood for an experiment which might be of value to the United States. This blood was to be collected at the Memorial Hospital in such a manner that half of it might be used as a source of serum and one-half used as a source of plasma and that each of these moieties could in turn serve

as a source of dried material which was to be prepared by Mr. Robert Folsom in a drying unit which he had constructed in order that comparative tests might be run to determine the efficacy of these blood substitutes from the same individuals on the same recipients. The job of preparing this serum and plasma for therapeutic trial was graciously accepted by Dr. William Thalhimer. Three sets of tests were to be carried out on each of these different materials. One set consisted of chemical and electrophoretic tests by Dr. Scudder of Presbyterian Hospital. The second type of testing was to be carried out by Dr. Chambers of New York University and it consisted of the perfusion of small mammals with serum or plasma and a recording of the effect on the capillaries as seen under direct observation. The third series of trials were to be clinical in nature and were to be carried out by Dr. Edward B. Self and Dr. John Scudder at the Presbyterian Hospital.

There was an insufficient number of donors for this specific purpose to get reliable data before the close of the "Plasma for Britain" project, but when the American Red Cross set up its first bleeding center in New York for the purpose of supplying dried plasma for our own army and navy an agreement was made with Dr. DeKline of the American Red Cross and Dr. Rhoads, representing the National Research Council, that the necessary bloods to continue this experimentation might be obtained. With this increased supply more definite results soon became available.

Dr. John Scudder has reported on the phase of the work which he undertook in an earlier paper in this program. Dr. Edward Self, associated with Dr. Scudder, has likewise reported his results following the clinical trial of both plasma and serum in a liquid form and dried form as well as serum in the fresh state as compared to serum several weeks old. I refer you to their papers for more complete discussion of this most important question and shall

only state here that it is the feeling of the Blood Transfusion Association that both plasma and serum when properly prepared are equally innocuous. Serum, however, does have definite advantages. These are: the protein contentvolume for volume is roughly 2% higher, it may be filtered with great ease through any type of bacterial filter, there is much less tendency for the material to become cloudy as the result of protein precipitation, and since there is no anticoagulant in serum it may be dried much more efficiently. For hospital blood banks it appears the part of wisdom to continue the use of plasma removed from blood which has become too old to use in the whole form.

The biological tests carried out by Drs. Robert Chambers, B. W. Zweifach, M. J. Kopac, and C. Hyman are, it seems, of real significance in assessing the properties of plasma and serum and with their permission I should like to include here their impressions to date. The full text of these experiments will be the subject of a future publication. The following is an outline of their methods and a summary of their findings to date:

"Perfusion of blood capillaries as a bio-assay method for the evaluation of transfusion media.

"Procedure:

Bio-assay technique.

Micromanipulative investigations on the blood capillaries of the mesentery have indicated that the responses of the small blood vessels to perfused fluids and to micro-operations can serve as a bio-assay method in determining the adequacy of various blood derivatives and substitutes which might be used in transfusion or in the treatment of shock. The technique consists of the perfusion of artificial media through various tissues in situ permitting microscopic observations simultaneous with micro-operations of the vessels with mechanically

controlled needles. The perfusions on the frog are made through the bulbus aortae so that a circulation is maintained through the entire animal.

"The present study deals with the perfusion of human citrated plasma and serum. Perfusions were also made with gelatin-Ringers to which citrate, in varying concentrations, was added in order to ascertain the specific effects of citrate alone.

"Observations to date have been restricted to the capillary circulation in the web, the tongue and especially the mesentery of the frog. The vessels of the capillary bed in these tissues are strikingly responsive to relatively slight alterations in the perfusion media. The ability or inability of these solutions to maintain the various aspects of the normal circulation thereby served as a preliminary index of the relative efficiency of the two blood substitutes.

"Materials.

"The human plasma and serum were obtained from Dr. Drew of the American Red Cross Blood Bank at the Presbyterian Hospital and were diluted with 0.15 per cent NaCl (40 cc. plasma to 60 cc. NaCl) to reduce the colloidal osmotic pressure to the level of that of the frog. It should be noted that this procedure reduced the concentration of the citrate to one-third that of the plasma as usually used for human transfusion purposes.

"The citrated plasma was obtained within a few hours after the phlebotomy and the cells were then removed by centrifugation. An occasional sample showed some hemolysis, these being segregated and treated as separate entities. The serum was obtained by allowing the fresh uncitrated plasma to clot for about 5 to 6 hours, after which the serum was decanted off without breaking the clot. Care was taken to avoid mixing the serum with cellular debris of the clot.

"In order to obtain an adequate distribution of the perfusate, it was

necessary to use particulate matter in the perfusion fluid (Zweifach, A. J. Physiol., 130: 512, 1940). Three types were used: (1) human red cells, (2) rooster red cells and (3) carbon particles. These were washed several times and suspended in saline. Hematocrit readings were made and precautions taken to eliminate samples containing hemolysed cells. The human red cells were used only with homologous plasma. The avian cells were found to survive better than human cells on storage in saline and were used when human red cells were unavailable. These cells could not be used with the serum samples because of the marked hemolytic effect of the latter on rooster red cells. Thus, the plasma perfusions were made with human and avian red cells and with carbon, while serum was used only with carbon as the particulate component.

"Determinations of the pH of the perfusion media were made with the Beckman glass electrode. The citrated plasma samples were usually alkaline (pH 7.9 to 8.2) and it was necessary to adjust the pH of these at least to about pH 7.8 with phosphate buffers.

"A mixture of oxygen and carbon dioxide was bubbled through the perfusate to maintain the necessary driving pressure and to aerate and stir the suspension. Such slow bubbling (about 1 bubble/second) produces a slight foaming so that, under normal perfusion conditions, a layer of froth about 2 cm. high rests on the surface of the liquid.

"It is well known that frothing, or the adsorption of proteins at oil-water interfaces, may change proteins from a soluble to an insoluble state. In fact, rapid frothing may actually bring about surface denaturation. It was important, therefore, to determine whether the bubbling of gas mixtures through the perfusates could produce significant changes in solubility of the plasma or serum proteins.

"A simple apparatus was constructed to permit (1) a very vigorous bubbling of a gas through the plasma and (2) a collection of the resulting froth.

"The results were: (1) There was no significant increase in turbidity of the recovered, protein-containing liquid phase of the foam. (2) The foaming was as pronounced after the fifth bubbling as initially observed. The latter finding indicates that the protein fraction remained surface active and hence the native state predominated. Preliminary tests with a du Nouy tensiometer also failed to show any changes (significant) in surface tension (liquid-gas) from untreated to bubbled plasma. The lack of any increase in turbidity indicates that the bubbled plasma did not gain in insoluble or denatured proteins.

"It is safe to conclude, therefore, that the amount of bubbling which the perfusate undergoes during the course of the perfusion experiment is far too low to produce any significant change in protein solubility.

"Criteria.

"The specific capillary responses were: (1) effect on the rate of blood flow and on the caliber of a, small arteries and veins, b, arterioles and venules and c, true and a-v capillaries; (2) development of a sticky exudate and the formation of intra-capillary thrombi; (3) permeability of vessels in the capillary bed by observing hemoconcentration, loss of retention of colloidal dyes, plastering of carbon and red cells against the wall and (4) development of stasis.

"The observations included responses of the vessels to micromanipulative prodding and trauma. Edema was noted grossly by observing visceral organs and extremities.

"The object of the investigation thus far is to detect the direct effects of citrated plasma and of serum, undiluted with the plasma of the host, on the circulatory system. Since the systemic reactions obtained by direct infusion into the intact circulation are not involved here, the results obtained may not be directly analogous with the results of transfusion studies, but they may indicate tendencies as to the relative values of the two types of transfusion media (plasma or serum).

"Results:

"Citrated plasma.

"Perfusion under a pressure of 30 to 40 mm. Hg. maintained normal circulation for 30 to 40 minutes during which no abnormal effects were observed on the capillaries which maintained their normal caliber and circulation. Impairment of the circulation after this initial period was occasioned by a failure at the venous outflow. The flow in the veins became increasingly sluggish and the lumina gradually filled with masses of red cells and sticky material. These veins became enormously distended and, although a slow flow persisted, the capillary bed was no longer efficiently drained. The arterioles remained patent and appeared normal. However, the perivascular smooth muscle elements in the entire capillary bed gradually lost their normal responsiveness to mechanical stimulation. After 15 to 20 minutes of perfusion the skeletal muscles went into tetany and then became non-responsive to nerve stimulation. The unresponsiveness to prodding of the smooth muscle of the capillary bed may be of the same order as that of the skeletal musculature.

"During the perfusion, observations in the web showed that the peripheral arterioles become constricted and completely shut off circulation within two to three minutes after the beginning of perfusion. Simultaneous observation

of the mesentery revealed that the mesenteric circulation was not affected except in those cases where the concentration of citrate was raised from 0.03 to 0.3 per cent whereupon the mesenteric arterioles and larger vessels underwent spasmodic contraction and became completely constricted.

"No differences were observed in the effects of fresh plasma (2 to 3 days) and stored plasma (2 to 3 weeks). The stored plasma usually had a delicate fibrous precipitate which was always removed by filtering before use.

"The toxic manifestations of the citrated plasma appear to be due largely to the citrate ion and to the lack of calcium. The citrate apparently acts adversely on muscle both striated and smooth. The lack of calcium prevents the cement elaborated by the endothelium from becoming deposited in a stable form without apparently preventing its secretion. As a result, a loose gelatinous material progressively accumulates in the venous vessels, thus increasing the viscosity of the fluid and enhancing the formation of red cell thrombi.

"Previous experiments have shown that alkalinity stabilizes the calcium proteinate which is a constituent of the intercellular cement. In the present experiments, the alkalinity of the citrated plasma, which was never below pH 7.8, tended to counteract the effect of the lack of calcium on the formed cement. This is in accordance with the known effect of pH on the calcium salt ionization which is decreased with increase in alkalinity. Continued perfusion with the alkaline citrated plasma actually toughens the wall of the capillaries and makes them highly resistant to mechanical handling with microneedles.

"<u>Serum</u>.

"Perfusions at pressures of 30 to 40 mm. Hg. maintained normal circulation

for several hours and proved superior to any of the previously used blood substitutes.

"The small arteries and arterioles maintained their normal tonic state and even exhibited normal rhythmic vasomotion during the period of observation. The arterioles also exhibited spontaneous contractions and dilations, frequently seen in intact circulation. The capillaries maintained their normal tone and contractibility as evidenced by microprodding. Severe prodding of the capillaries produced the usual sticking of carbon locally, a phenomenon not found when citrated plasma was used.

"During the several hours of observation (in some cases 4 to 5 hours) the capillaries maintained their normal impermeability to the colloidal dye T1824 (so-called Evans Blue).

"The skeletal muscles responded to nerve stimulation, the heart continued to beat, and no gross edema was evident in any of the organs. In the dye perfusion experiments, the T1824 circulated through all tissues including the skin. This effect was not obtained when citrated plasma was used.

"In contrast to the above findings are the results obtained when hemolyzed material (hemoglobin plus cellular debris) was added to the serum and to citrated plasma. The mixture with serum was extremely toxic, the effects appearing within 5 to 10 minutes of perfusion (extreme spasm of the arteries, varicose appearance of the veins). On the other hand the mixture with plasma was no more toxic than the citrated plasma alone, except that capillary stasis appeared before venous back pressure became evident.

R. Chambers
B. W. Zweifach
M. J. Kopac
C. Hyman

May 22, 1941
Department of Biology
Washington Square College of Arts and Science
New York University"

This biological assay gives evidence of the superiority of serum over plasma which is more striking than the clinical evidence though both seem to indicate that the serum is a more physiological substance and therefore causes less reaction of an unfavorable nature on the part of the recipient. One might bring the discussion of this problem up to date by stating that all of our data at this time suggests that stored plasma or serum may be used with freedom from reactions and with the expectation of good clinical results in shock, hemorrhage, and hypoproteinemia but that the advantage seems to lie on the side of serum rather than on the side of plasma as we thought less than a year ago. Serum from freshly clotted blood, however, does have an increased reaction rate.

8. Dried Plasma and Serum. Dried serum and dried plasma, as prepared by Mr. Robert Folsom of Memorial Hospital in New York City by the apparatus which he has already described to you as a part of this large scale experimental program, in Dr. Self's hands have proved almost equally efficacious in combatting the clinical conditions for which they are indicated. The reaction rates were low in each instance and quite comparable. The electrophoretic and chemical changes in this material has been reported on by Dr. Scudder in an earlier chapter. There is the tendency, it appears, for the reaction rate to go up with the concentration of the material and it would seem to be a wise precaution to use isotonic material, be it plasma or serum, liquid or dried, unless there be specific indications for hypertonic fluids.

PLANS FOR A NATIONWIDE COLLECTION OF BLOOD AND PLASMA FOR USE BY THE ARMED FORCES OF THE UNITED STATES OR BY THE AMERICAN RED CROSS IN CASE OF NATIONAL CATASTROPHIES

In the report of the Blood Transfusion Association of January, 1941 a plan was submitted for the establishment of a nationwide system of collecting

blood for the preparation of dried or liquid blood substitutes. On February 3 at the Presbyterian Hospital in New York City the American Red Cross set up, under the direction of its New York Chapter, the first unit in such a system. Utilizing the experience gained in the "Plasma for Britain" project a small full time staff was obtained to collect the blood and the Sharpe & Dohme plant in Glenolden, Pennsylvania was chosen as the laboratory for processing the plasma and dispensing it in the dried form. In March the first mobile unit for the collection of blood was tried out and found to add so much to the possibilities of reaching civilian donors that the program now goes on at an increased pace under the American Red Cross and its many local chapters in many scattered parts of the country.

This project "Plasma for Britain" had two objects, the first, to aid England in a very dark hour, the second, to make available increased information in the field to our own government and its armed forces. Both, we believe, have been at least in part achieved.